

**Table S1:** Extended version of **Table 1:** Includes binding-site amino acid differences as an alignment, and as binding site conservation percentage. Includes references to previous reports on antifungal activity for other fungi.

Drug	IC50	Identified human target(s)	UniProt code	Predicted fungal target(s) (UniProt code)	Binding-site amino acid differences *	Binding site conservation (%)	References		
							Other reports in fungi	Inhibitory Concentration	Reference
Miglitol	>386	Maltase-glucoamylase, intestinal	O43451	F0UFH1	DTTNYDIIWWDMSFRWDTDFARH ·AYI···M····A····L··G··	69,6	---	---	---
Pemetrexed	131	Thymidylate synthase	P04818	F0URV8	RTVKRVFEKIWNFYSLHDGLGPFNYTIKMMAV ··L········Y·T········G····S·	84,4	<i>C. albicans</i>	IC50= 1 µM	[1]
Myricetin	16	Dual specificity mitogen-activated protein kinase 1	Q02750	F0UFI3 F0UAN5 F0U908	NGGKILLIVGFIMDCDFGVSLIM ·Y······ID··V······VI ······G··TVL······ATVI A·····N·CRY········FTD	73,9 65,2 65,2	<i>C. albicans</i> <i>H. capsulatum</i>	20 µg/ml 36 µM	[2] [3]
Cobimetinib	<3,2						<i>H. capsulatum</i> <i>F. oxysporum</i> <i>A. fumigatus</i>	12.5 µM 65 µM 82 µM	[3]
GDC0623	47						<i>H. capsulatum</i> <i>C. neoformans</i> <i>A. fumigatus</i>	63 µM 82 µM 7 µM	[3]
TAK-733	>397						<i>C. neoformans</i> <i>A. fumigatus</i>	198 µM 54 µM	[3]
Refametinib	<0,3						<i>H. capsulatum</i> <i>C. neoformans</i>	17.5 µM 54 µM	[3]
Trametinib	>49	Dual specificity mitogen-activated protein kinase 1	Q02750	F0UFI3 F0UAN5 F0U908	NGGKILLIVGFIMDCDFGVSLIM ·Y······ID··V······VI ······G··TVL······ATVI A·····N·CRY········FTD	73,9 65,2 65,2	<i>Not effect at the tested concentrations for:</i> <i>H. capsulatum</i> <i>C. neoformans</i> <i>C. albicans</i> <i>C. parapsilosis</i> <i>F. oxysporum</i> <i>A. fumigatus</i>	>49	[3]
AZD 6244	>328						Dual specificity mitogen-activated protein kinase 2	P36507	F0UFI3 F0UAN5 F0U908
Mycophenolic Acid	2,8	Inosine-5'-monophosphate dehydrogenase 2	P12268	F0UKI1	SPMNRGSGSICITDGGIMMGSLSYGMGSQG ········A········G········	93,1			
Ribavirin	>410						<i>C. albicans</i>	MIC80= 2 µg/ml - 8 µg/ml	[5]
							<i>Multiple Candida strains (63)</i> <i>C. albicans</i>	MIC = 0.37 - 3.02 µg/ml	[6]

Drug	IC50	Identified human target(s)	UniProt code	Predicted fungal target(s) (UniProt code)	Binding-site amino acid differences *	Binding site conservation (%)	References		
							Other reports in fungi	Inhibitory Concentration	Reference
							<i>C. parapsilosis</i> <i>C. tropicalis</i>		
							<i>C. krusei</i> , <i>C. glabrata</i> <i>C. lusitaniae</i> <i>C. albicans</i> strains	MIC ≥24.16 µg/ml	
							<i>C. albicans</i> strains	MIC50 = 2-8 µg/ml	[7]
Azathioprine	>180						---	---	immunosuppressant
Atorvastatin	<0,4	HMG-CoA reductase	P04035	F0UKH1	EGCLSRRMNSEVSNCDKKKAHNSLALGHLH ··V·	96,7	<i>C. albicans</i> <i>C. glabrata</i>	MIC = 4-8 µg/ml MIC = 4-8 µg/ml	[8]
Fluvastatin	0,3						<i>C. albicans</i>	MIC < 1 µg/ml	[9]
Eflornithine	>338	Ornithine decarboxylase	P11926	F0U9K9	AKCDAPRLHSGGGFEPGRCY ·	100,0	<i>A. fumigatus</i>	256 µg/ml	[10] (However, it was considered to have no antifungal effect)
Risedronate	>262	Farnesyl pyrophosphate synthase	P14324	F0UP55	FFLADDMDRTEQDKTFYQDDKDK ··S·	91,3	<i>Cryptococcus</i> strains	Geometric mean MIC = 378.49 mg/l	[11]
Carbidopa	>164	Aromatic-L-amino-acid decarboxylase	P20711	F0UAU0 F0UHL5	SASHSTGTDAYNHK ·	85,7 78,6	---	---	---
Olaparib	>184	Poly [ADP-ribose] polymerase 1	P09874	F0UEN3	QELDNLDEVWHGSNQGLRIAPAPTGYGKGIYFAKSY K·ETT·I·	83,3	---	---	---
Rucaparib	233	Poly [ADP-ribose] polymerase 2	Q9UGN5	F0UEN3	SIQEWHGSIHGLRIAPGYGGIYFAKSY KVE·Q·	82,8	---	---	---
Atovaquone	0,23	Dihydroorotate dehydrogenase	Q02127	F0UDX1	MAYLMLQLDPEAHLAFTLLPFLMVRVYYTLTG Y·AIV·IY·A·AGCM·H·L·L·L·V·  Ligand binding site, the sites for orotate and FMN have higher conservation percentages, but are not shown.	50	<i>A. fumigatus</i> <i>F. oxysporum</i>	MIC = 3-0.6 µM MIC = 0.001- 0.06 µM	[12]
Leflunomide	<23	Dihydroorotate dehydrogenase	Q02127	F0UDX1	MAYLMLQLDPEAHLAFTLLPFLMVRVYYTLTG Y·AIV·IY·A·AGCM·H·L·L·L·V·	50	---	---	---
		Protein-tyrosine kinase 2-beta	Q14289	F0U6P0	LGEGVAKKSEIMLIVMELYGELHLLGDFR V·K·N·YV·S·K	75,9			

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Cilastatin	>279	Dipeptidase 1	P16444	F0UPY1	YEHHRNYDGV .....TF...M	75	---	---	---
Dasatinib	>205	Tyrosine-protein kinase Fyn	P06241	F0UAN5 F0UR08 F0UT49	LGNVAKEVTEYMGSANLAD ..A.....M.....S..C. ..K.....M..L.NE..... ..S.....M..I.T...S.	78,95 73,7 73,7	---	---	---
Disulfiram	31	Aldehyde dehydrogenase, mitochondrial	P05091	F0UNE9  F0UNE9 F0U4T1 F0URF3	VMFNFLMWTELFCCCALYDVFFE (site1) INS.....NMI..  IIPWNMWKVAEQFGPGAFTGSIVIELGGCQKEIFLF (site2) .....T.....R.....VQ.....R..... .....A.....K.....TQ..T...R..... .GA..I..PS.Y.T-.....QTKV.....H.....V	75  86,5 83,8 62,2	<i>C. albicans</i>  <i>C. auris</i>	IC50 = 1 µM  IC50 = 1 µM	[13]
Entacapone	>655	Catechol O-methyltransferase	P21964	F0UET8	WMNVKEGAYGYSIEINCRFGASQFDHWKDRDNC Y.....G....L.R.FML.T.D...Y.PA..S.	61,8	---	---	---
Febuxostat	>253	Xanthine dehydrogenase/oxidase	P47989	F0UCF6	EGGLKLVVGNTTEIILALWFAVVASGGNITISDLLILKDD .....I.G.S..T...Y..I..A..A.....V...	76,9	---	---	---
L-Glutathione	>122	Glutathione reductase	P00390	F0UFI2	CVVYTIR .....  (Glutathione site)	100	---	---	---
Paclitaxel	>59	Tubulin beta-3 chain	Q13509	F0UCQ9 F0UQK5 F0U6N3 F0USZ5	GQCQIDEGGNSGGGTGVPVDTENLYLN ..... ..A....DS.....NTS..I... ..A.L.DDA.....TA..V... ...NV.....A.....A.VN..FT.	100 74,1 70,4 70,4	---	---	---
Sacubitril	>232	Neprilysin	P08473	F0UAA0	RVNAFYIFMVHEHEDVWCCTYVHGR E...Y...S.....AKM..Q.	72	---	---	---
Aliskiren	>164	Renin	P00797	F0U899	TQYVDGSWVPAHLYVVMFPLAFDGVYDTGASMA A.....I.LAEA.FG...IL...T..D	63,6	<i>C. albicans</i>	2 mg/ml	[14]
Dexrazoxane	>373	DNA topoisomerase 2-beta  DNA topoisomerase 2-alpha	Q02880  P11388	F0UWA9	PKEGDLRGKILNAEQM .....L.....Q  IFTSSNGGRNGYGAKTQK V.S.....	87,5  88,9	<i>Nematocida parisii</i>	60 µM  (Spore growth inhibition)	[15]
Bufexamac	184	Histone deacetylase 6	Q9UBN7	F0UKK7 F0UVW7	DHHP SHHGFDHFDLGY VG..V..... PL.....Y....	81,25 81,3	---	---	---
Baricitinib	198	Tyrosine-protein kinase JAK1  Tyrosine-protein kinase JAK2	P23458  O60674	F0UW57 F0UR08 F0USL5  F0UR08 F0UAT6 F0UP18	DLGEGGKVAKVMEFLPSGSKEDRNVLGD .....AI...IL...L.D-..N.L.A. -..K..T.....Y..L.NAD.E.I.A. -I...S....L.YV.G..AM.A...S.  LGKGGSVAKVAMEYLPKSDKRNLDIFWYAPLW .....T.....N.QE..A.--YV..... I...R...RL..I...S.D..S.V..M..V. ..S..T...TK...G...PA..A...M..I.	64,3 62,96 62,96  69,7 66,7 66,7	---	---	---

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							Other reports in fungi	Inhibitory Concentration	Reference
		Protein-tyrosine kinase 2-beta	Q14289	F0U6P0	LGEGVAKKSEIMLIVMELYGELHLLGDFR V·K·.....N·.....YV·.....S··K	75,9			
Tofacitinib	>198	Tyrosine-protein kinase JAK1	P23458	F0UW57 F0UR08 F0USL5	DLGEGGKVAKVMEFLPSGSKEDRNVLGD .....AI·...IL·...L·D-...N·L·A· -·K·T·.....Y·L·NAD·E·I·A· -I·...S·...L·YV·G·AM·A·...S·	64,3 62,96 62,96	---	---	---
		Tyrosine-protein kinase JAK2	O60674	F0UR08 F0UAT6 F0UP18	LGKGGSVAKVAMEYLPGSDKRNLDIFWYAPLW .....T·.....N·QE·A·--YV·..... I·...R·...RL·I·S·D·S·V·M·V· ·S·T·TK·...G·PA·A·--M·I·	69,7 66,7 66,7			
Filgotinib	>235	Tyrosine-protein kinase JAK1	P23458	F0UW57 F0UR08 F0USL5	DLGEGGKVAKVMEFLPSGSKEDRNVLGD .....AI·...IL·...L·D-...N·L·A· -·K·T·.....Y·L·NAD·E·I·A· -I·...S·...L·YV·G·AM·A·...S·	64,3 62,96 62,96	---	----	---
Upadacitinib	>263						---	---	---
Ellagic acid	>83	Protein kinase C alpha type	P17252	F0UE28 F0UP18 F0U6P0 F0U745 F0UBW5	LGKFFVAKETMEYVDDNMAD .....L·...I·...L· ·S·.....LSA·L· V·.....NV·...E·LS· IS·.....A·L·LT· I·.....V·FL·LT·	84,2 73,7 68,4 68,4 68,4			
Vorinostat (SAHA)	7	Histone deacetylase 2	Q92769	F0UUK7 F0UKC3	YMRDFAGGLHHGFCDHFDLGGY ..... F·...YS·.....	100 87	<i>A. fumigatus</i> <i>A. flavus</i> <i>A. terreus</i>	MIC > 16 µM	[16]
		Histone deacetylase 6	Q9UBN7	F0UKC3 F0UUK7 F0UVW7	DHHPSHHGFDHFDLGY -S·F·..... VG·V·..... PL·.....Y·...	84,6 81,25 81,3			
podophyllotoxin	>241	DNA topoisomerase 2-alpha	P11388	F0UWA9	IFTSSNGGRNGYGAKTQK V·S·.....	88,9			
Cholic acid	>245	Ferro chelatase, mitochondrial	P22830	F0UF14	NMGGFLLFLMLPILFIRRIYSIYSSTHSLPVYVSGPMWAFHI .....Y·...II·GL·L·.....S·.....	83,3	<i>C. albicans</i>		[17]
Dronedarone	3,9	Brain cyclic nucleotide-gated channel 1/2 (BCNG-1)/ BCNG-2	O60741/ Q9UL51	F0UKN4	IVMLFGEICRRTAVR ·V·...VV·.....	80	---	---	---
Nintedanib	<9	Fibroblast growth factor receptor 3	P22607	F0UGV1 F0UUJ8	LGEGFGVAKIVEYANRNLDLDR .....R·L·EE·-- I·D·...VM·M·E·...	78,95 70	---	---	---
Lenvatinib	>234					---	---	---	
Ivabradine	>198	Potassium/sodium hyperpolarization-activated cyclic nucleotide-gated channel 2	Q9UL51	F0UKN4	IVMLFGEICRRTAVR ·V·...VV·.....	80	----	----	----

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Enasidenib	20	Mitochondrial isocitrate dehydrogenase (IDH2)	P48735	F0UJM9	TLDQKLGEAAHGTVTRHSTND .....	100  54%	---	---	---
Entrectinib	11	Proto-oncogene tyrosine-protein kinase 1 ROS1	P08922	F0UW59	LGVEAKLLELMEGDTRNCLGD .....AP·ENE·I·A·	66,7	----	----	---
		Neurotrophic receptor tyrosine kinase 1 (NTRK1)	P04629	F0UL15	LGEFGVAKVFEYMRHGDRRNCLGDFGMSR ...YA.....F·-DK·Q·L.....LA·	65,5			
		Tyrosine-protein kinase JAK2	O60674	F0UR08 F0UAT6 F0UP18	LGKGGSVAKVAMEYLPGSDKRNLDIFWYAPLW .....T.....N·QE·A·--YV..... I.....R.....RL·I·S·D·S·V·M·V· ·S·T·TK·G·PA·A·M·I·	69,7 66,7 66,7			
		Neurotrophic receptor tyrosine kinase 2 (NTRK2)	Q16620	F0USL5 F0UUJ8 F0U6B1	LGFVAKELLIVFEYMKHGLFHRNCLIGDFM I.....L·VPG·I·A·V·S·I I.....L·M·D--I·E·I·A·L ·K.....L·QQ·CNS·S·VS·-	66,7 66,7 65,5			
Larotrectinib	>233	Neurotrophic receptor tyrosine kinase 1 (NTRK1)	P04629	F0UL15	LGEFGVAKVFEYMRHGDRRNCLGDFGMSR ...YA.....F·-DK·Q·L.....LA·	65,5	---	---	---
		Neurotrophic receptor tyrosine kinase 2 (NTRK2)	Q16620	F0USL5 F0UUJ8 F0U6B1	LGFVAKELLIVFEYMKHGLFHRNCLIGDFM I.....L·VPG·I·A·V·S·I I.....L·M·D--I·E·I·A·L ·K.....L·QQ·CNS·S·VS·-	66,7 66,7 65,5			

\* It is important to remember that these amino acid strings do not correspond to contiguous positions in the protein sequence but rather to the set of amino acids that shape the binding pocket, determined based on structural criteria [3].

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